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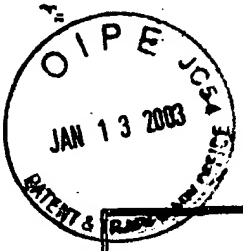

PATENT
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I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Tracy Simmons — Tracy Simmons
Printed name of person mailing correspondence — Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Ralph A. Nixon et al.	Art Unit:	1632
Serial No.:	09/560,124	Examiner:	Anne-Marie Baker
Filed:	April 28, 2000	Customer No.:	21559

Title: METHODS FOR THE IDENTIFICATION OF COMPOUNDS FOR THE TREATMENT OF ALZHEIMER'S DISEASE

Commissioner For Patents
Washington, D.C. 20231

DECLARATION OF DR. RALPH NIXON UNDER 37 C.F.R. § 1.132 TRAVERSING GROUNDS OF REJECTION

Under 37 C.F.R. § 1.132, I declare:

1. I am an inventor of the subject matter described and claimed in the above-captioned parent application.

2. I have read the Office Action mailed July 8, 2002.

3. We have successfully reduced to practice the overexpression of rab5 in mice. Specifically, we have now demonstrated that mice overexpressing rab5 exhibit endosomal changes that resemble changes observed in Alzheimer's disease. The successful acute overexpression of rab5 in mouse brains was achieved using Herpes

Simplex Virus (HSV) infection *in vivo*. This overexpression persisted for at least ten days and involved cell populations at a considerable distance from the injection site. When highly overexpressed, rab5 was largely cytoplasmic. At lower expression levels rab5 was present in endosomes, which were substantially enlarged. Given these results, one skilled in the art would predict that rab5 transgene expression, driven by appropriate promoters, will enlarge endosomes in rab5 overexpressing transgenic mice.

4. The results of these studies are shown in Exhibit A, panels A-E. Panels A and B are photomicrographs showing rab5 immunostaining in striatal neurons of sectioned mouse brains. Panel A shows low levels of rab5 present in striatal neurons in wild-type mouse brain. Panel B shows high levels of rab5 immunostaining in mouse brain sectioned three days after an HSV vector driving rab5 (HSV-rab5) expression was injected into the cingulate cortex. Panel C is a photomicrograph showing rab5 immunostaining in enlarged endosomes visualized using Nomarski optics in an HSV-rab5 injected mouse. The enlarged endosomes present in rab5 overexpressing mice resemble endosomal changes observed in Alzheimer's disease. Panels D and E are photomicrographs showing rab5 immunostaining in human pyramidal neurons. Panel D shows rab5 immunostaining in endosomes of a normal brain. Panel E shows rab5 immunostaining in endosomes of a human brain with Alzheimer's disease.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Date: 1/03/03

Dr. Ralph Nixon

21559

PATENT TRADEMARK OFFICE